THE DILEMMA OF HEREDITARY PROSTATE CANCER

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Abstract • Résumé

The observation that a family history of prostate cancer significantly increases a man's risk of the disease (see pages 895 to 900 of this issue) highlights many of the ethical, emotional and pragmatic controversies in medical circles concerning the management of this common form of cancer. This editorial describes a patient's personal dilemma when he learns that his brother is dying of prostate cancer, a dilemma that illustrates the potential harms and benefits of early detection and treatment. Current evidence does not justify screening asymptomatic men for prostate cancer, but many Canadian physicians do practise early case detection for some patients with a high risk of the disease. Men with a family history of prostate cancer must be informed by their physicians about the known and unknown risks and benefits of early detection and treatment, before they undergo the cascade of diagnostic and therapeutic procedures associated with prostate cancer.

L'observation selon laquelle des antécédents de cancer de la prostate dans la famille augmentent considérablement le risque d'un homme d'être atteint de la maladie (voir pages 895 à 900 du présent numéro) est le point saillant d'un grand nombre des controverses éthiques, psychologiques et pragmatiques qui règnent dans les milieux de la médecine au sujet du traitement de cette forme répandue de cancer. Cet éditorial décrit le dilemme personnel d'un patient lorsqu'il apprend que son frère est sur le point de mourir d'un cancer de la prostate, dilemme qui illustre les préjudices et les avantages possibles d'un dépistage et d'un traitement précoces. Les preuves actuelles ne justifient pas le dépistage du cancer de la prostate chez les hommes qui ne présentent aucun symptôme, mais beaucoup de médecins canadiens pratiquent le dépistage précoce chez certains patients à risque élevé. Les médecins doivent informer les hommes qui ont des antécédents de cancer de la prostate dans leur famille des risques et des avantages connus et inconnus que présentent le dépistage et le traitement précoces avant qu'ils se soumettent à la batterie d'interventions diagnostiques et thérapeutiques liées au cancer de la prostate.

"My brother has prostate cancer." An empathetic and experienced physician can sense the anxiety and even fear in his or her patient who asks about his chances of inheriting this dreaded disease. The physician would like to reassure the patient that prostate cancer is primarily a disease of older men and that more men die with it than from it. However, prostate cancer can be a killer, especially if it develops in younger men. It is the most common form of cancer, and the second most common cause of death from cancer, among men.[1] An article in this issue by McLellan and Norman (see pages 895 to 900) confirms reports on the familial clustering and mendelian inheritance pattern of some prostate cancer. This simple and valuable observation highlights many of the ethical, emotional and pragmatic questions concerning our present approach to the management of prostate cancer.

A PATIENT WITH PROSTATE CANCER

There have been serious controversies and well-argued differences of opinion on the appropriate diagnosis and management of prostate cancer during the last decade. The most relevant issues, including the hereditary aspects of the disease, were brought home for me by a recent encounter with a patient. He was a lawyer, 49 years of age, whose brother, who was 12 years older, was dying of prostate cancer in a nearby city. My patient was a healthy man who had no symptoms of prostate disease, yet he was concerned about reports on prostate cancer in the press, and he feared that he was also harbouring the disease.

I discussed with him at length the recent controversy in medical circles concerning whether asymptomatic men should be screened for prostate cancer. The Canadian

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Task Force on the Periodic Health Examination has recommended that the test for the serum level of prostate-specific antigen (PSA) not be used routinely in asymptomatic men for the early detection of prostate cancer.[2] In its guidelines the Canadian Urological Association has recommended that the test for the serum PSA level not be offered as a screening test for prostate cancer except in the context of a randomized trial.[3] I also told him the newest information, that men with a family history have a significantly higher risk of prostate cancer than the asymptomatic population discussed in the screening controversy. Testing for prostate cancer was the only way to determine my patient's risk of having the disease; it could improve his chances for his survival if indeed he had it. It was imperative that he know not only that this approach had not been proven in clinical trials but also that the diagnosis and treatment of prostate cancer could adversely affect his quality of life. My practice is to conduct early, specific case detection rather than screening all asymptomatic men. I subscribe to the view that all men who are at high risk of prostate cancer, who have symptoms or who are concerned about prostate cancer developing be offered a digital rectal examination (DRE) and a test for the serum PSA level. This particular patient fit two of these categories. A DRE showed that his prostate was small and benign. However, a DRE alone is a poor predictor of prostate cancer, unless the result is obviously abnormal.[4] Following lengthy discussions, my patient agreed to further investigations. His serum PSA level was 4.0 ng/mL, which was within the range considered normal by our laboratory. However, according to recent evidence on age-specific ranges of PSA levels[5] his result would be in an elevated category (the normal range is 0.0 to 2.5 ng/mL for men 40 to 49 years of age). He underwent a transrectal ultrasonographic (TRUS) examination of his prostate, which showed a hypoechoic area 1 cm in diameter in the peripheral zone of the left lobe of his prostate. A TRUS-directed transrectal needle biopsy of the prostate confirmed the presence of a Gleason 6/10 (moderate grade) adenocarcinoma in the hypoechoic area. Random biopsies of the rest of the prostate had negative results.

The patient was a lawyer, trained to ferret out the truth by weighing the evidence gathered by asking insightful questions:

"Had I known I was at high risk of prostate cancer, could I have prevented it?

"Shouldn't my own doctor have screened me for prostate cancer?

"When should my son be checked for prostate cancer?

"Can I be cured?

"What is it going to cost me to be cured?"

Unfortunately, the evidence is not all available, the jury is hung, and the verdict is still unclear.

Prevention

To prevent prostate cancer we must know what causes it. In their article McLellan and Norman allude to some of the factors that may be associated with it. These include geography, occupation, fertility, sexual activity, infectious agents, race, education level, diet and sex-hormone levels. The ultimate goal of epidemiologic studies is to identify real risk factors for prostate cancer and to use this knowledge for prevention strategies. At present we have no idea how to prevent prostate cancer through lifestyle modification or preventive intervention, although a trial funded by the National Cancer Institute of chemoprophylaxis with finasteride, a 5α-reductase inhibitor, is now under way in the United States. A total of 18 000 men older than 55 years of age will be randomly assigned to receive finasteride or a placebo to determine whether inhibition of dihydrotestosterone synthesis in the prostate for a prolonged period decreases the incidence of prostate cancer.[6]

The article in this issue confirms that there is a significantly higher risk of prostate cancer among men with a family history of the disease. This important observation must be exploited to effect secondary cancer prevention in this high-risk group.

Early detection

Screening with DRE and the test for the serum PSA level have not yet been shown to reduce the rate of death from prostate cancer.[2] Yet, for individual patients, the only strategy available to minimize their risk of dying of prostate cancer is early detection and treatment. Testing high-risk men is not really screening but, rather, early case detection. On the basis of the data presented in McLellan and Norman's review, men with at least one first-degree relative with prostate cancer may now be encouraged to have an annual DRE and a test for the serum PSA level, starting at an earlier age than that advocated by proponents of screening. McLellan and Norman suggest that testing of these patients should start at 40 years of age.

The two tests now used for screening and early detection of prostate cancer are not ideal. The DRE, although simple to perform and inexpensive, has a low sensitivity and positive predictive value in detecting prostate cancer in asymptomatic men.[4] Measurement of the serum PSA level is the most accurate predictor of prostate cancer available and remains the best indicator of cancer progression, but it is not the ideal marker for occult cancer. The sensitivity and specificity of serum PSA levels, used alone as a screening test, are limited. However, 33% of men with a serum PSA level greater than 4.0 ng/mL are found to have a tumour upon biopsy.[7] New approaches

to the evaluation of the serum PSA level in individual men, including age-specific ranges of serum PSA levels, PSA density, PSA velocity and the measurement of bound and free PSA, will likely improve the accuracy of this simple and inexpensive test.

Given the prevailing negative view of screening we must be careful not to extrapolate from this view to the point of discouraging case detection in high-risk groups. A combination of the inexpensive and noninvasive DRE and test for serum PSA level seems to be the most cost-effective method of early case detection in men at high risk of prostate cancer. Such case detection should be offered only to men whose health and age do not preclude an attempt at curative therapy (i.e., the men should have an expected 10 to 15 years or more to live).

Treatment of early prostate cancer

Does contemporary treatment of early prostate cancer in young men reduce mortality? An aggressive program of early case detection among men with a family history of prostate cancer, as McLellan and Norman advocate, should lead to an increased diagnosis of earlier-stage prostate cancer in this population. These relatively young men will undoubtedly be subjected to the most widely advocated treatment for early-stage disease in men their age, a radical prostatectomy.

Some controversial studies of a program of watchful waiting (or benign neglect) in men with prostate cancer have suggested that the disease does not have a significant effect on longevity.[8] However, a recent reappraisal of this population shows that over 10 to 15 years prostate cancer does result in significant mortality.[9] Half of the patients who presented with prostate cancer that had not metastasized ultimately died of it; of the patients who were alive 10 years after their first diagnosis 63% eventually died of the disease. There are no data from well-designed randomized prospective trials showing that patients with localized prostate cancer benefit from early treatment in terms of overall mortality or mortality due to cancer.[10]

By contrast, numerous surgical case series have shown that the median survival of patients who undergo a radical prostatectomy to treat localized cancer is longer than 15 years, and observed crude survival rates are the same as those among men without prostate cancer.[11] But surgical treatment exacts its toll. Death due to the operation is a remote possibility, and the effect of long-term complications such as impotence and incontinence on quality of life is almost impossible to calculate. Recent advances in surgical technique and greater experience in conducting the procedure, along with better selection of patients and a trend toward younger patients, has reduced the early mortality rate to 0.28%,[12] the total urinary incontinence rate to 0.8%[13] and the partial incontinence rate to 8%.[14] Furthermore, 68% of men (and 91% of men less than 50 years of age) who were potent before the operation retain their potency.[15] Although it is less popular for treating younger men, radical radiotherapy also offers a potential cure, with less morbidity than radical surgery.[16]

A patient's dilemma

In light of the evidence presented by McLellan and Norman it now becomes the responsibility of physicians to take into account any family history of prostate cancer when assessing all men over 40 years of age. Physicians must offer each patient with family members with prostate cancer up-to-date, accurate information on the detection and treatment of this type of cancer. The patient's concern about prostate cancer, his age and any coexisting illnesses must be taken into account. The physician's role, then, is to discuss the increased risk of prostate cancer among men with a strong family history, the reliability of our current detection techniques and the risks and benefits of detecting and treating localized prostate cancer. This information must be accurate and adequate. The patient too must assume a role in decision making. He should assess the information about screening, diagnosis and treatment provided by his physician so that he can make an informed decision whether to be tested for prostate cancer.

My patient, the lawyer, researched the topic, asked critical questions and carefully assessed the arguments of the proponents and opponents of early diagnosis and treatment. He realized that although prostate cancer cannot be prevented and screening is generally not recommended a rational argument could be made for case finding in men at high risk of the disease, starting at 40 years of age for his son. He decided that the best way to minimize his risk of dying of prostate cancer was to detect it early. He eventually had a radical retropubic prostatectomy and, for him, the minimal complications he suffered were worth the potential benefit of being cured of prostate cancer.

Physicians who are committed to early diagnosis and treatment of prostate cancer, and men who undergo diagnostic tests and treatment, must believe that the patient's brother, who died of prostate cancer in his 60s, was once a 50-year-old man with a curable disease.

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Conferences continued from page 916

Nov. 9–10, 1995: Canadian Coordinating Office for Health Technology Assessment 5th Regional Symposium — Economic Evaluation: Its Role in Decision Making

Vancouver

Conference coordinator, Canadian Coordinating Office for Health Technology Assessment, 110–955 Green Valley Cres., Ottawa ON K2C 3V4; tel 613 226-2553, fax 613 226-5392

Les 9 et 10 nov. 1995 : 5e symposium régional de l'Office canadien de coordination de l'évaluation des technologies de la santé — L'évaluation économique : son rôle dans la prise de décision

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Les 9 et 10 nov. 1995 : 8e Congrès annuel de l'Association des médecins spécialistes en santé communautaire du Québec: La santé publique et la promotion des mesures efficaces

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Du 9 au 11 nov. 1995 : 2e conférence nationale sur l'asthme et l'éducation (organisée par l'Université Laval)

Québec

Crédits de l'éducation médicale continue.

A. Les McDonald, directeur exécutif, Réseau canadien pour le traitement de l'asthme, 1607–6, Forest Laneway, Willowdale ON M2N 5X9; tél 416 224-9221, fax 416 224-9220

Nov. 9–11, 1995: 2nd National Conference on Asthma and Education (hosted by Université Laval)

Quebec City

Study credits available.

A. Les McDonald, executive director, Canadian Network for Asthma Care, 1607–6 Forest Laneway, Willowdale ON M2N 5X9; tel 416 224-9221, fax 416 224-9220

Nov. 10–11, 1995: Partners in Progress, incorporating the Pediatric Oncology Group of Ontario Annual Multidisciplinary Symposium on Childhood Cancer: Diagnosis, Treatment and Beyond, and Canada's 3rd Pediatric Oncology Nursing Conference: the Vital Link — Trends and Transitions

Toronto

Keynote speaker: Janet Beed, Ontario Cancer Institute

Pediatric Oncology Group of Ontario, 700–620 University Ave., Toronto ON M5G 2C1; tel 416 592-1232, fax 416 592-1285

Nov. 10–12, 1995: Emergency Cardiac Care Educational Symposium — Communities: the Ultimate Coronary Units

Toronto

Zabelle Barbarian, conference secretary, Health Promotion Dept., Heart and Stroke Foundation of Ontario, 4th floor, 477 Mount Pleasant Rd., Toronto ON M4S 2L9; tel 416 489-7111, ext 431; fax 416 481-3439

Nov. 13–14, 1995: From Hospital to Community: Working Together to Support Breastfeeding (sponsored by La Leche League Canada)

Ottawa

Agnes Vargha, 25 Bernier Terr., Kanata ON K2L 2V1; tel 613 592-2379, fax 613 599-7298

Nov. 15–17, 1995: 7th International Symposium: Caring for Survivors of Torture — Challenges for the Medical and Health Professions

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